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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/985,822	11/06/2001	Eamon Brady	08157.0021	4538
7590	06/16/2004		EXAMINER	
Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P. 1300 I Street, N.W. Washington, DC 20005-3315			NAFF, DAVID M	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/985,822

**Applicant(s)**

BRADY ET AL.

**Examiner**

David M. Naff

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-108 is/are pending in the application.
- 4a) Of the above claim(s) 47-108 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                                                           |                                                                                         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                                                               | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                                                      | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>1/6/01 &amp; 3/23/04</u> . | 6) <input type="checkbox"/> Other: _____                                                |

**DETAILED ACTION**

In a response of 3/23/04 to a restriction requirement of 9/24/03, applicants elected Group I claims 1-46 without traverse, filed a supplemental preliminary amendment amending the specification, and submitted replacement formal drawings containing Figures 1-17.

Replacement Figures 1-17 will be entered and considered by the draftsman.

Claims 47-108 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/23/04.

Claims examined on the merits are 1-46.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C.

112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and where required in other claims, "cellular material" (lines 2 and 3 of claim 1) is uncertain as to meaning and scope in defining structure of the scaffold. It is uncertain how "cellular" defines scaffold structure in addition to the voids

Art Unit: 1651

interconnected by pores required in claim 1. If cellular is requiring cells, it is uncertain where the scaffold contains the cells in addition to the voids and pores. The specification does not describe cells in addition to voids and pores. It is suggested that "cellular" be deleted unless it can be established that this term is defining structure in addition to the voids interconnected by pores, and the claims are made clear as to the additional structure defined by cellular.

Claim 3 is unclear and improper by depending on a plurality of claims. The claim should recite "in any preceding claim" in place of "in the preceding claims".

Claims 7-46 are confusing and unclear and are improper multiple dependent claims by being a multiple dependent claim and depending on another multiple dependent claim, or by depending on a multiple dependent claim that depends on another multiple dependent claim.

In claim 7, --- claim --- should be inserted after "preceding" to be clear.

Claims 10-14 are unclear by requiring or further limiting cells or a cell and not having antecedent basis for the scaffold of claim 1 containing cells in addition to the voids and pores required. It is uncertain as to the relationship of the cells of these claims to the voids and pores of claim 1. The specification does not describe cells in addition voids and pores. The reference to cells should be deleted unless it can be made clear where the scaffold contains cells in relation to the voids and pores interconnecting the voids.

Art Unit: 1651

In claim 10, the structure is uncertain of a cell that is three-dimensional with fattened faces at points of contact between cells. Additionally, it is uncertain as where these cells with contact points exist in relation to the voids and pores of claim 1.

Claims 12-14 are unclear where the pores that interconnect cells exist in the scaffold in relation to the pores of claim 1 that interconnect voids.

Claim 15 is unclear whether the pores required are the pores that interconnect voids of claim 1 or some other pores.

In claim 16, the meaning and scope of "solubility parameter" is uncertain. This term has not been defined in the specification. If the term is used the prior art and has a known art recognized meaning when expressed as MPa, evidence of this should be provided. Additionally, the meaning of "MPa<sup>0.5</sup>" is uncertain. What does the abbreviation "MPa" stand for? Furthermore, the term "MPa<sup>1/2</sup>" is used in claim 23 to denote "cohesive energy density". How can "MPa" represent both "solubility parameter" and "cohesive energy density"?

Claim 17 is confusing by requiring the cellular material to contain both a soft phase and a hard phase. Since the scaffold comprises the cellular material, it appears the cellular material is a solid since the scaffold is a solid, and it is not seen how a scaffold in solid form can contain a soft phase and a hard phase as separate phases. It appears soft and hard phases exist only in a process of making the scaffold as disclosed in the specification (pages 47-50) where a polyol resin which is a soft phase is mixed with an isocyanate

Art Unit: 1651

resin which is a hard phase. After mixing and reaction of the resins, there are no longer separate and distinct phases which can be labeled as soft and hard. See the specification at page 49, lines 15-18, where it is disclosed that two incompatible phases are interspersed to bring reactive sites into close proximity to facilitate reactions. The reaction appears to be between the polyol preparation (page 48) and the isocyanate preparation (page 47). After mixing and reacting and curing (page 51, lines 1-8)) which allows all reactive sites to react, it is not seen how the resulting polymer can contain two distinct and separate phases with one hard and the other soft.

In claims 18 and 19, "polar ratio" is uncertain as to meaning and scope. Claim 18 should contain the definition of the term as in the specification (paragraph bridging pages 23 and 24) by before the period in line 2, inserting --- , wherein the polar ratio is the ratio of carbon atoms to the sum of nitrogen and oxygen atoms contained by the polyurethane polymer ---. With this change , line 2 of claim 1 should be amended by inserting --- polymer --- after "polyurethane".

Clear antecedent basis is not found for "the polymer" in line 1 of claims 18 and 19. The insertion of polymer in line 2 of claim 1 as set forth above will provide antecedent basis.

In claim 23, there is not clear antecedent basis for "the cohesive energy density".

The term "hard segment context" in claim 22 and the term "cohesive energy density" in claim 23 are uncertain as to meaning and scope. The terms have not been defined in the specification. If

Art Unit: 1651

terms are used in the prior art and have an art recognized meaning, and the former is known to be expressed as percent as in claim 22 and the latter is known to be expressed as MPa as in claim 23, evidence of this should be supplied.

Requiring the scaffold to contain a hard phase and soft phase in claim 23 is confusing for reasons set forth. As set forth above, in view of the specification it appears such phases exist only with respect to phases mixed to prepare the scaffold.

In claims 24-26, there is not clear antecedent basis for "the leachables". The claims should require the polyurethane polymer to contain leachables and the content claimed be present after extracting the polymer with water.

In claim 27, line 3 should be changed to read --- 4,4 diphenyl methane diisocyanate (MDI) containing a 2,4 diphenyl methane diisocyanate isomer --- to be clear and consistent with the specification (page 39).

In claims 35, 36 and 44-46, "mass" should be replaced with --- weight --- to be clear since weight and not mass is measured to obtain the percent values recited.

In claims 35, 36, 39, 41 and 46, there is not clear antecedent basis for "the reaction formulation" since a reaction formulation has not been previously required.

In claims 39 and 40, there is not clear antecedent basis for "the isocyanate index". Additionally, "isocyanate index" is uncertain as to meaning and scope. This term has not been defined in the

Art Unit: 1651

specification. If this term is used in the prior art and has an art recognized meaning in relation to values recited, evidence of this should be supplied.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26 and 39-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brady et al (6,177,522 B1) in view of Holy et al (6,379,962 B1), and if necessary in further view of Agrawal et al (6,187,329 B1) or Brekke (4,186,448) or Barrows et al (5,856,367).



Art Unit: 1651

The claims are drawn to a tissue engineering scaffold comprising a porous polyurethane cellular material having a plurality of voids interconnected by pores, wherein the cellular material has a void content of 85 to 98% and a surface area to volume ratio of from 5 to 400 mm<sup>2</sup>/mm<sup>3</sup>.

Brady et al disclose preparing porous polycarbonate urethane polymer such as a polyurethane foam for implanting in the body (col 1, lines 6-11). The polycarbonate urethane is based on diol, diamine, water and chain extenders (col 8, lines 12-15). Foams of lowest density are prepared by a combination of water blown reaction, in a depressurized reactive/forming vessel with the incorporation of a physical blowing agent into the formulation (paragraph bridging cols 8 and 9). A quasiprepolymer system can be used where some of the polyol is reacted with the isocyanate to generate an isocyanate terminated prepolymer in an excess of isocyanate, and remaining polyol and chain extender is subsequently added (col 9, lines 22-26). The isocyanate can be diphenylmethane diisocyanate (col 5, line 29), and a chain extender can be 1,4 butanediol (col 10, line 57). Carbon dioxide generated as a byproduct forms a cellular structure, and with the use of a surfactant the size and porosity of the cellular structure can be controlled (col 8, lines 40-46). The void space can be at least 80% (col 10, lines 40-43). Density can be controlled independently of the hard segment content by controlling the pressure of the reaction/forming chamber (col 8, lines 50-52).

Holy et al disclose a polymer scaffold having a macroporous network with macropores having microporous struts as walls. The porosity is greater than 85% (col 6, line 61).

Agrawal et al disclose a polymer matrix for implanting having a porosity of 1-99% and particularly 75-99% (col 14 lines 15-20).

Brekke discloses a polymer material for implanting having about 90% voids (col 1, line 44 and paragraph bridging cols 1 and 2).

Barrows et al disclose a porous matrix for implanting having a void volume of 20-97% (col 14, lines 40-42).

When preparing the polyurethane polymer material having a cellular structure as disclosed by Brady et al, it would have been obvious to provide the cellular structure with a porosity of greater than 85% as disclosed by Holy et al, and if necessary as further suggested by Agrawal et al, Brekke or Barrows et al disclosing polymer implants having a porosity or void volume that can be higher than 85% since Brady et al disclose a void space of at least 80% (col 10, line 43) and producing foams of lowest density (col 8, lines 65-67) that inherently have a high void volume as claimed. The cellular structure in the form of a foam of Brady et al when having a void content as set forth above will inherently contain a plurality of voids interconnected by pores, and a surface area to volume ratio as claimed. The limitations of dependent claims are inherent in Brady et al, or would have been obvious from Brady et al in combination with the other references.

Art Unit: 1651

Claims 27, 28, 31-36 and 39-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-26 and 39-46 above, and further in view of Hanson (4,687,482) and Tabor (5,478,867).

The claims require manufacturing the scaffold using diphenyl methane diisocyanate containing less than 3% 2,4 isomer, a linear long chain diol which is free of tertiary carbon linkages, water, a cross-linking agent, a trimerisation catalyst, a blowing and/or gelling catalyst and a surfactant.

Hanson disclose making a polyurethane polymer for implanting using polytetramethylene ether glycol (col 6, line 53).

Tabor discloses using a trimerization catalyst in preparing a porous polyurethane foam polymer to lower density and compressive strength of the foam (col 6, lines 31-49). The catalyst can be potassium acetate (col 6, line 46).

When preparing the polyurethane foam of Brady et al as set forth above, it would have been obvious to use polytetramethylene ether glycol as the diol as suggested by Hanson and a trimerization catalyst as suggested by Tabor. Using diphenyl methane diisocyanate containing less than 3% 2,4 isomer would have been obvious to us a pure diphenyl methane diisocyanate.

***Claim Rejections - 35 USC § 103***

Claims 27, 29-36 and 39-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-26 and 39-46 above, and further in view of Reich et al (5,993,972) and Tabor.

Art Unit: 1651

Claims 29 and 30 require the diol of claim 27 to be a polycarbonate diol.

The invention of claim 27 and Tabor are described above.

Reich et al disclose using a polycarbonate diol (for example see col 6, line 13) in preparing a polyurethane polymer that can be implanted (col 5, line 42).

When preparing the polyurethane foam of Brady et al as set forth above, it would have been obvious to use a polycarbonate diol as the diol as suggested by Reich et al and a trimerization catalyst as suggested by Tabor. Using diphenyl methane diisocyanate containing less than 3% 2,4 isomer would have been obvious to us a pure diphenyl methane diisocyanate.

***Claim Rejections - 35 USC § 103***

Claims 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 27, 28, 31-36 and 39-46 or claims 27, 28, 31-36 and 39-46 above, and further in view of Jamiolkowski et al (6,147,168).

The claims require a trialkanol amine cross-linking agent.

Jamiolkowski et al disclose using triethanolamine (col 11, line 49) when carrying out polymerization in preparing a polyurethane polymer that can be used as an implant.

When preparing the polyurethane foam of Brady et al as set forth above, it would have been obvious to use triethanolamine as a cross-linking agent as suggested by Jamiolkowski et al.

***Double Patenting***

Claims 1-26 and 39-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,177,522 in view of Holy et al, and if necessary in further view of Agrawal et al or Brekke or Barrows et al.

Claims of the patent are drawn to a polycarbonate urethane article that can be a foam prepared by reacting a polycarbonate polyol, an isocyanate, water and a chain extender.

For the type of reasons set forth above, it would have been obvious to provide the foam of the patent claims with a porosity of greater than 85% as disclosed by Holy et al, and if necessary as further suggested by Agrawal et al, Brekke or Barrows et al disclosing polymer implants having a porosity or void volume that can be higher than 85% and since claim 8 requires a void space of at least 80%. A foam of the patent claims when having a porosity or void space as set forth above will inherently have a plurality of voids interconnected by pores and a surface area to volume ratio as claimed.

The conditions of dependent claims will be obvious in view of the claims of the patent and Holy et al, and if necessary in further view of Agrawal et al, Brekke or Barrows et al.

***Double Patenting***

Claims 27, 28, 31-36 and 39-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,177,522 in view of

Art Unit: 1651

Holy et al, and if necessary in further view of Agrawal et al or Brekke or Barrows et al as set forth above under obvious double patenting, and further in view of Hanson and Tabor for the type of reasons above when applying these references.

When preparing the urethane foam of the claims of the patent as set forth above, it would have been obvious to use polytetramethylene ether glycol as the diol as suggested by Hanson and a trimerization catalyst as suggested by Tabor. Using diphenyl methane diisocyanate containing less than 3% 2,4 isomer would have been obvious to us a pure diphenyl methane diisocyanate.

#### ***Double Patenting***

Claims 27, 29-36 and 39-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,177,522 in view of Holy et al, and if necessary in further view of Agrawal et al or Brekke or Barrows et al as set forth above under obvious double patenting, and further in view of Reich et al and Tabor for the type of reasons above when applying these references.

When preparing the urethane foam of the claims of the patent as set forth above, it would have been obvious to use a polycarbonate diol as the diol of the patent claims as suggested by Reich et al and a trimerization catalyst as suggested by Tabor. Using diphenyl methane diisocyanate containing less than 3% 2,4 isomer would have been obvious to us a pure diphenyl methane diisocyanate.

***Double Patenting***

Claims 37 and 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,177,522 in view of references as applied to claims 27, 28, 31-36 and 39-46 or claims 27, 28, 31-36 and 39-46 above under obvious double patenting, and further in view of Jamiolkowski et al for the type of reasons above when applying this reference.

When preparing the urethane foam of the patent claims as set forth above, it would have been obvious to use triethanolamine as a cross-linking agent as suggested by Jamiolkowski et al.

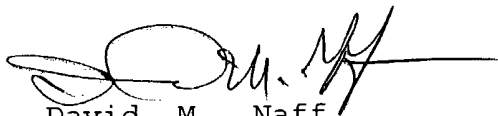
***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1651

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff  
Primary Examiner  
Art Unit 1651

DMN  
6/10/04